REMARKS

Claims 1-39 are all the claims pending in the application. Claims 14 and 31-39 have been withdrawn from consideration; claims 1-7, 13 and 15-30 are rejected; claims 8-12 are objected to.

A number of amendments have been made to the claims in response to suggestions made by the Examiner, and to more clearly state that which Applicants regard as their invention.

In each instance where an additional element was introduced into a claim, there is clear support in the specification for the amendment. Such instances include the following:

Claim 1 - the addition of the subscripts "x" and "y" and the definitions thereof find support in the claims as filed where it is stated that R^1-R^2 and R^3 are a number of amino acids.

Claim 13 - support of the addition of the terms "radioactive" and "fluorescent" to describe the tag and label, respectively, is found at page 11, lines 26-32.

New claims 40 and 41 find support in claims 35 and 26, respectively, and the understanding by the skilled artisan that inflammation and septic shock may be caused by bacteria.

New claim 42 finds support in the specification at page 10, lines 27-28.

New claim 43 finds support in claim 23, as filed.

New claim 44 finds support in claim 28. as filed.

New claims 45-47 find support in the specification at page 5, lines 1-2, and lines 18-19.

Accordingly, no new matter has been added and Applicants respectfully request entry of the amendment.

I. Formal Matters

In response to the Notice of Draftperson's Patent Drawing Review, Applicants proffer to submit revised drawings upon allowance of one or more claims in the application.

II. Restriction Requirement

At page 2 of the Office Action, the Examiner acknowledges Applicants' election with traverse of Group I, i.e., claims 1-7, 11, 13, and 15-30. The Examiner found Applicants' traversal unpersuasive, and therefore made the restriction final.

In response, while Applicants do not further contest the Restriction Requirement at this time, they maintain their traversal of the Restriction Requirement, and reserve the right to file a petition to the Commissioner, after final action on or allowance of claims to the invention elected, but no later than appeal. A request to reconsider the Restriction Requirement was made in the Response to Restriction Requirement filed June 14, 2001. 37 C.F.R. § 1.144.

At page 3 of the Office Action, the Examiner states that it is recognized that the five BP peptides (SEQ ID NO: 1-5) have the core sequence of the formula (R^1-R^2-A-B-(A-B-C-A)$_m$-(C)$_n$-R^3), and has therefore withdrawn the election of species requirement.

As a result, claims 1-13 and 15-30 are under active consideration.

III. Claim Objection

At paragraph 1 of the Office Action, claims 8-12 are objected to.

The Examiner stated that the term "SEQ ID NO." is improper, because a colon (":") should be used in place of a period (".").

In response, Applicants have amended the claims to replace "SEQ ID NO." with "SEQ ID NO:" Accordingly, Applicants respectfully request reconsideration and withdrawal of this objection.

IV. Claim Rejection under 35 U.S.C. §101

At paragraph 2 of the Office Action, claim 1 is rejected under 35 U.S.C. § 101.

The Examiner contends that claim 1 is drawn to a peptide but does not explicitly indicate the "hand of man." The Examiner suggests the insertion of "purified" in connection with the peptide.

In response, Applicants have amended claim 1 as suggested by the Examiner. Accordingly, Applicants respectfully request reconsideration and withdrawal of this objection.

V. Rejection under 35 U.S.C. § 112, first paragraph

At paragraph 3 of the Office Action, claims 1-7, 13 and 15-30 are rejected under 35 U.S.C. §112, first paragraph.

A. Beginning on page 4, the Examiner acknowledges that the specification is enabling for the 8 specific BP peptides disclosed in the specification. However, the Examiner contends that the specification does not reasonably enable all peptides of the general formula (R^1-R^2-A-B-(A-B-C-A)$_m$-(C)$_n$-R^3). Specifically, the Examiner contends that Applicants fail to disclose any data to indicate that all of the peptides of formula (R^1-R^2-A-B-(A-B-C-A)$_m$-(C)$_n$-R^3) have stable α-helix structures. The Examiner contends that various peptides, comprised of amino acid combinations that satisfy the formula (R^1-R^2-A-B-(A-B-C-A)$_m$-(C)$_n$-R^3), could predictably have β-sheet structures rather that α-helices. The Examiner cites Gly-Arg-Tyr-Arg-

Ile-Tyr-Arg-Arg-Ile-Tyr-Arg-Arg-Tyr-Ile-Arg-Ile-Ile-Ile-Gly as an example of a peptide of formula (R^1-R^2-A-B-(A-B-C-A)$_m$-(C)$_n$-R^3) which the Examiner alleges would have a β-sheet structure rather than an α-helix.

In response, Applicants submit concurrently herewith the executed Declaration of one of the inventors, Dr. Philip Richard ABRAHAM. As clearly set forth in the Declaration, (1) the skilled artisan would expect that each peptide that conforms to the formula recited in the claims would form a stable α-helix because there is no peptide falling within the definition recited in the claim that would not adopt an α-helical structure, and (2) the peptide proposed by the Examiner (page 5, lines 2 and 3, of the Office Action), would <u>not</u> form a β-sheet.

Dr. Abraham further demonstrates that the specification enables the skilled artisan to make and/or use the invention commensurate in scope with the claims. Applicants note that the claims are directed to a purified peptide with clearly defined characteristics. The characteristics only require that peptides be of the recited formula, and that they are amphipathic, cationic and form a stable α-helix.

In view of the evidence presented in the Declaration, Applicants assert that the skilled artisan would be enabled to practice the full scope of the claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of this portion of the rejection.

B. In the first full paragraph of page 5, the Examiner further asserts that the specification does not provide data to support the breadth of claims 15-27.

The Examiner explains that the specification has not demonstrated that a pharmaceutical composition comprising a peptide of formula (R^1-R^2-A-B-(A-B-C-A)$_m$-(C)$_n$-R^3) is useful for

treating *fungus, virus or parasite infection, or treating topic and systemic tumors, inflammation or septic shock, or the treatment being prophylactic.* The Examiner states that the specification only discloses peptides such as BP1, BP2, BP2.1, and BP2.2 as having antibacterial activity.

In response, Applicants again refer to the Declaration of Dr. Abraham (*see, especially*, page 6-10). Therein, experimental evidence is provided demonstrating that the peptides of the consensus formula can be used for each of the purposes recited in the claims relating to the treatment of infections by bacteria, the prevention of inflammation or septic shock, and as a prophylactic.

In addition, experimental evidence reported therein demonstrates that peptides of the consensus formula can be used for each of the purposes recited in the claims relating to the treatment of infections by viruses and parasites, or the treatment of local and systemic tumors.

Moreover, included therein are experimental results from experiments showing the efficacy of using peptides of the consensus formula in clearance of bacteria from human whole blood samples, thus showing the peptides to be effective in humans.

Thus, in view of the Declaration evidence, Applicants assert that undue experimentation would not have been required to practice the present invention, and therefore, in view of the Declaration evidence, respectfully request reconsideration and withdrawal of the rejection.

C. In the first full paragraph of page 6, the Examiner contends that there is insufficient data to demonstrate that a peptide of formula (R^1-R^2-A-B-(A-B-C-A)$_m$-(C)$_n$-R^3) effectively treats microbial infection in *humans*. The Examiner states that Applicants only disclose the administration of BP2 to mice.

In response, Applicants once again refer to the Declaration of Dr. Abraham (*see, especially*, page 10-12). Therein is a discussion of the correlation between mouse models and treatment of humans, as well as additional evidence demonstrating that a peptide of formula (R^1-R^2-A-B-(A-B-C-A)$_m$-(C)$_n$-R^3) effectively treats microbial infection in humans. In view of the Declaration evidence, Applicants respectfully request reconsideration and withdrawal of this portion of the rejection.

VI. Claim Rejections under 35 U.S.C. § 112, second paragraph

At paragraph 4 of the Office Action, claims 1, 6-7, 13 and 15-30 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite.

The Examiner states that the phrases "R^1-R^2 and R^3 are a number of amino acids" and "wherein one or more of the repetitive sequence motifs (A-B-C-A)" render claim 1 indefinite. The Examiner states that the number and identity of R^1-R^2 and R^3 are unclear, as is the number of repetitive sequence motifs (A-B-C-A) that are in the formula.

In response, claim 1 has been amended to delete the phrase "R^1-R^2 and R^3 are a number of amino acids" and instead recite R^1, R^2, and R^3 each as an amino acid, and to add x and y subscripts to the formula, thereby defining, for each R group, the number of moieties.

As to the Examiner's rejection of the phrase "wherein one or more of the repetitive sequence motifs (A-B-C-A)", Applicants assert that it is clear from the claim that there are between 2 and 8 copies of the motif. However, in order to more clearly recite Applicants' invention, claim 1 has been amended by deleting "repetitive" from the rejected phrase.

Accordingly, Applicants respectfully request reconsideration and withdrawal of this portion of the rejection.

Claims 2 and 3

At paragraph 5, the Examiner rejects claims 2 and 3 as indefinite for use of the phrase "R^1-R^2 and R^3 each have a number of amino acids ranging from 0 to 15." The Examiner states that the peptide is unclear, specifically, how many amino acids and what kind of amino acids are R^1-R^2 and R^3.

In response, Applicants have amended claims 2 and 3 to clearly recite the number and identity of the amino acids recited in the phrase "R^1-R^2 and R^3 each have a number of amino acids ranging from 0 to 15."

Accordingly, Applicants respectfully request reconsideration and withdrawal of this portion of the rejection.

Claims 5, 15 and 21

At paragraph 6, the Examiner rejects claims 5, 15 and 21 as indefinite because of the term "and/or".

In response, Applicants have amended claim 5 to replace the phrase "wherein R^1-R^2 and/or R^3 does not" with "wherein R^1-R^2 or R^3, or both, do not comprise." Applicants have amended claims 15 and 21 in a similar fashion.

Accordingly, Applicants respectfully request reconsideration and withdrawal of this portion of the rejection.

Claim 6

At paragraph 7, the Examiner rejects claim 6 as indefinite because of use of term "more often than." Specifically, the Examiner states it is unclear how more often (A-C-B-A) occurs than (A-B-C-A).

In response, Applicants have amended claim 6 to replace the phrase "more often than" with "greater than."

Accordingly, Applicants respectfully request reconsideration and withdrawal of this portion of the rejection.

Claim 13

At paragraph 8, the Examiner rejects claim 13 as indefinite for use of the term "a non-peptide carrier, tag or label" stating that it is unclear what kind of carrier, tag or label the peptide is coupled to.

In response, Applicants assert that the meaning of the term "non-peptide carrier, tag or label" is readily apparent to one skilled in the art, as defined in the specification at page 11, lines 28-32. Therein, it is stated that such components are useful for tracing the peptide, *in vivo* and *in vitro*, and allow for the identification and quantification of binding of the peptide to substrates. It is also stated that such compounds are well-known in the art and include, for example, biotin, and radioactive and fluorescent labels.

However, in order to more clearly recite the elements of claim 13, claim 13 has been amended to recite a "radioactive" tag and a "fluorescent" label.

Accordingly, Applicants respectfully request reconsideration and withdrawal of this portion of the rejection.

Claim 21

At paragraph 9, the Examiner rejects claim 21 as indefinite because of the use of the term "a mixture of at least two peptides according to claim 1." The Examiner is unclear as to how many peptides and how much of each peptide is included in the mixture.

In response, Applicants assert that the skilled artisan would understand that the number and proportion of the two or more peptides in the mixture is irrelevant. The invention can be practiced with any number and any proportion. Thus, Applicants assert that the claim is not indefinite as written.

Accordingly, Applicants respectfully request reconsideration and withdrawal of this portion of the rejection.

Claim 22

At paragraph 10, the Examiner rejects claim 22 as indefinite because of the use of the term "derivatives or analogues." The Examiner states that it is unclear what kind of antibiotics are intended as compared to the parent compounds.

In response, Applicants have deleted the term "derivatives or analogues" from claim 22.

Accordingly, Applicants respectfully request reconsideration and withdrawal of this portion of the rejection.

Claim 29

At paragraph 11, the Examiner rejects claim 22 as indefinite for use of the term "has or can have occurred". The Examiner contends it is unclear whether the trauma or suspected infection has occurred or not.

In response, Applicants respectfully note that the Examiner is mistaken in that claim 22 does not contain the term "has or can have occurred." However, claim 29 does use this term, therefore Applicants proceed under the assumption that the Examiner meant to recite claim 29 in this rejection. Further, Applicants have amended claim 29 to delete the term "or can have."

Accordingly, Applicants respectfully request reconsideration and withdrawal of this portion of the rejection.

Claim 23

At page paragraph 12, the Examiner rejects claim 23 as indefinite because of the phrase "such as".

In response, Applicants have amended claim 23 to delete the phrase "such as the parasite causing malaria or Trypanosomiosis", and instead recite these parasites in a new claim 43, dependent from claim 23.

Accordingly, Applicants respectfully request reconsideration and withdrawal of this portion of the rejection.

Claims 28-30

At paragraph 13, the Examiner rejects claims 28-30 as indefinite, stating that they lack essential steps as claimed in the process of treating a mammal suffering from microbial infection. The Examiner lists the missing steps as: the site and method of administration, the therapeutically effective amount of peptide and a step whereby the desired outcome and length of treatment using the peptide can be determined.

In response, Applicants have amended claim 28 to recite "mammals in need of such treatment" and "a therapeutically effective amount."

As to the Examiner's additional requirements for site and method of administration and length of treatment, Applicants assert that these are unnecessary limitations, especially in the absence of any cited prior art. Indeed, such limitations are not critical elements of Applicants' claimed invention.

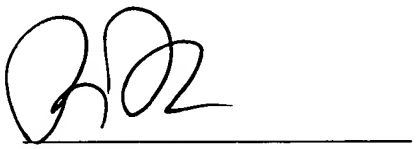
Accordingly, Applicants respectfully request reconsideration and withdrawal of this portion of the rejection.

VII. Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

Applicant hereby petitions for any extension of time which may be required to maintain the pendency of this case, and any required fee, except for the Issue Fee, for such extension is to be charged to Deposit Account No. 19-4880.

Respectfully submitted,



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APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

The claims are amended as follows:

1. (Amended) A purified peptide comprising at least 12 amino acids, the peptide having an amino acid composition such that the peptide is amphipathic, cationic and forms a stable α-helix and is represented by the following formula (1) or the retro orientation of formula (1)~~has the following formula~~:

$(R^1\text{-}R^2)_x\text{-A-B-(A-B-C-A)}_m\text{-(C)}_n\text{-}(R^3)_y$ (1) ~~$R^1\text{-}R^2\text{-A-B-(A-B-C-A)}_m\text{-(C)}_n\text{-}R^3$;~~

wherein

R^1, R^2, and R^3 each are an amino acid,

x is an integer ≥ 0,

y is an integer ≥ 0,

each A is an amino acid independently selected from the group consisting of ~~basic amino acids~~ Lys, Arg and His,

each B is an amino acid independently selected from the group consisting of ~~aromatic amino acids~~ Phe, Trp and Tyr,

each C is an amino acid independently selected from the group consisting of ~~hydrophobic amino acids~~ Leu, Ile, Val and Ala,

m is an integer ~~a number~~ of from 2 to 8,

n is an integer ~~a number~~ of from 1 to 3, and

wherein one or more of the ~~repetitive~~ sequence motifs (A-B-C-A) may have the retro orientation (A-C-B-A)~~,~~

~~R^1 R^2 and R^3 are a number of amino acids,~~

~~said peptide having either the orientation according to the formula or the retro orientation thereof~~.

2. (Amended) The purified peptide according to claim 1, wherein ~~in which~~ x and y are each an integer of from 0 to 15~~R^1 R^2 and R^3 each have a number of amino acids ranging from 0 to 15~~.

3. (Amended) The purified peptide according to claim 1, wherein ~~in which~~ x and y are each an integer of from 1 to 10~~R^1 R^2 and R^3 each have a number of amino acids ranging from 1 to 10~~.

4. (Amended) The purified peptide according to claim 1, wherein R^1 is selected from the group ~~of sequences~~ consisting of:

ACAA, wherein each A and C is as independently ~~as~~ defined in claim 1;

Gly_p, wherein p is an integer of from 0 to 10; ~~p = 0-10~~ and

Ala_q, wherein q is an integer of from 0 to 10 ~~q = 0-10~~.

5. (Amended) The purified peptide according to claim 1, wherein R^1-R^2 or ~~and/or~~ R^3, or both, do ~~does~~ not comprise an amino acid selected from the group consisting of ~~from those of~~ A, B and ~~or~~ C as defined in claim 1.

6. (Amended) The purified peptide according to claim 1, wherein motifs (A-C-B-A) are present in said peptide in a greater amount than motifs (A-B-C-A)~~the repetitive sequence (A-~~

~~B-C-A) is present in the retro-orientation more often than in the orientation as presented in the formula~~.

7. (Amended) The purified peptide according to claim 1, wherein n = 3.

8. (Twice amended) The peptide BP 1, having SEQ ID NO: 1 ~~SEQ ID NO. 1~~.

9. (Twice amended) The peptide BP 2, having SEQ ID NO: 2 ~~SEQ ID NO. 2~~.

10. (Twice amended) The peptide BP 2.3, having SEQ ID NO: 3 ~~SEQ ID NO. 3~~.

11. (Twice amended) The peptide BP 2.4, having SEQ ID NO: 4 ~~SEQ ID NO. 4~~.

12. (Twice amended) The peptide BP 2.5, having SEQ ID NO: 5 ~~SEQ ID NO. 5~~.

13. (Twice Amended) The purified peptide according to claim 1, wherein the peptide is coupled to a non-peptide carrier, radioactive tag or fluorescent label.

14. (Amended) A fusion peptide comprising the peptide of claim 1 coupled to a second peptide selected from the group consisting of ~~form~~ peptide carriers and diagnostic peptides.

15. (Amended) A pharmaceutical composition comprising a peptide according to claim 1 as active component for treating topical and systemic microbial or ~~and/or~~ parasite infection, or both, and a pharmaceutically acceptable carrier in a pharmaceutically acceptable dosage form.

21. (Amended) A pharmaceutical composition comprising a mixture of at least two peptides according to claim 1 as active components for treating topical and systemic microbial or ~~and/or~~ parasite infections, or both, and a pharmaceutically acceptable carrier in a pharmaceutically acceptable dosage form.

22. (Amended) The pharmaceutical composition according to claim 15, further comprising an antibiotic selected from the group ~~class~~ consisting of penicillins, cephalosporins, ß-lactams, aminoglycosides, quinolones, tetracyclines, macrolides, glycopeptides or lipopeptides, hydrophobic antibiotics, ribosome inhibitors or antibiotics having a large lipid-like lactone ring~~, or derivatives or analogues thereof~~.

23. (Amended) The pharmaceutical composition according to claim 15, wherein the infection is caused by a parasite ~~such as the parasite causing malaria or Trypanosomiosis~~.

28. (Amended) A method for~~of~~ treatment of microbial infection in a mammal ~~including a human suffering from microbial infection~~, comprising administering to a mammal in need of such treatment a therapeutically effective amount of a peptide according to claim 1 ~~in a pharmacologically acceptable form to said mammal~~.

29. (Amended) The method according to claim 28, wherein said treatment is applied after trauma or suspected infection has ~~or can have~~ occurred.

Claims 40-47 are added as new claims.